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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/[illegible],[illegible]	[illegible]	PETERSON	[illegible]

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PENNIE & EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK NY 10036-2711

EXAMINER	
BRUSCA,J	

ART UNIT	PAPER NUMBER
1639	15

DATE MAILED: 08/10/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No. 08/986,186	Applicant(s) Peterson et al.
	Examiner John S. Brusca	Group Art Unit 1636

☒ Responsive to communication(s) filed on *6/2/99*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *27-50* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *27-50* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6, 8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This Supplemental Office Action is being sent because the Office Action mailed 7/14/99 was mistakenly based on the claims of the Amendment received 10/15/98, which was not entered. This Supplemental Office Action is based on the pending claims after entry of the Amendment received 6/2/99. The Office regrets any inconvenience this may have caused the Applicants.

Continued Prosecution Application

2. The request filed on 6/2/99 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/986186 is acceptable and a CPA has been established. An action on the CPA follows.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2).

However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

Nucleic acid sequences appear on pages 85, 86, and 104 and in the Brief Description of the Drawings of Figures 5A-5G, 6C, and 10 but applicants have not submitted a Sequence Listing as set forth in 37 CFR § 1.821 (see MPEP § 2422).

Applicants are required to comply with all of the requirements of 37 CFR § 1.821 through 1.825. Any response to this office action which fails to meet all of these requirements will be considered non-responsive. The Applicant's attention is directed to the attached Notice to Comply with the Sequence Rules. The nature of the sequences disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 34, 35, 41, 42, 45, 47, 49, and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes a method of making a biased combinatorial gene expression library comprising DNA fragments isolated from a plurality of species of organisms in which the selection is by hybridization to nucleic acid probes. The described probes listed on pages 63-64 are polyketide biosynthetic loci probes, actinorhodin biosynthesis (actI) probes, spore pigment biosynthesis probes (whiE), erythromycin biosynthesis probes (eryA1), antibiotic or secondary metabolism biosynthetic loci probes, peptide synthetase gene probes; thiostrepton, virginiamycin, valinomycin, and actinomycin biosynthetic loci probes; peptide synthase probes, and aminoglycoside synthase probes. The specification does not provide written support for probes of biosynthetic genes for: mevalonic acid, glucose transfer systems, beta lactams, macrolides, alkaloids, bryostatins, carotenoids, steroids, retinoids, tetracycline, oxytetracycline, puromycin, doxyrubicin, taxol, chloramphenicol, nalidixic acid, mithramycin, novobiocin, vulpinic acid, usnic acid, kainic acid, podophyllotoxin, brevitoxin, camptothecin, or artemisinin.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (f) he did not himself invent the subject matter sought to be patented.

8. Claims 27-34, 36-41, 43-46, and 48-50 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the donor organism is from an environmental sample from soil, deposits near hot springs or thermal vents, freshwater or seawater filtrates, or marine or estuarine sediments. In some embodiments the library is in a host cell. In some embodiments the selection is performed by hybridization to a secondary metabolism gene. In some embodiments the secondary metabolism gene is involved in antibiotic synthesis; thiostrepton, virginiamycin, valinomycin, or actinomycin synthesis.

U.S. Patent No. 5,824,485 shows throughout a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the constructs are operably linked to elements that allow for expression in a host cell. Columns 13-14 provide guidance to isolate donor organisms from an environmental sample from soil, deposits near hot springs or thermal vents, freshwater or seawater filtrates, or marine or estuarine sediments. Columns 31 and 32 provide guidance to make selected libraries that encode proteins that are involved in secondary metabolism, such as genes involved in the synthesis of antibiotics, polyketides, actinorhodin, spore pigment, erthromycin, thiostrepton, virginiamycin,

valinomycin, actinomycin, aminoglycosides, and peptides by peptide synthases. Column 19 provides guidance to use vectors selected from plasmids, cosmids, phagemids, viral vectors, and artificial chromosomes for introduction of the library into host cells.

Therefore U.S. Patent No. 5,824,485 anticipates the claimed invention. U.S. Patent No. 5,824,485 has a different inventive entity than the instant application.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 27-29, 32-36, 39-42, and 44-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21 and 22 of U.S. Patent No. 5,783,431 in view of Vining.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different

organisms. In some embodiments the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the selection is by hybridization to secondary metabolism genes, and the library is in a host cell.

Claims 21 and 22 of U.S. Patent No. 5,783,431 are drawn to a method of making a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the constructs are operably linked to elements that express the sequence in a host cell. Claim 22 is drawn to the method of claim 21 in which the selection is by hybridization to a metabolic pathway gene. Claims 21 and 22 of U.S. Patent No. 5,783,431 are not drawn to libraries selected for sequences that encode proteins that are involved in secondary metabolism.

Vining shows in the abstract that secondary metabolism genes are preferably isolated from genomes of different organisms because they are of ancient origin and are better conserved between species of organisms than within related genes of the same organism. Vining shows throughout many examples of secondary metabolism genes involved in the synthesis of polyketides, beta-lactams, and erythromycin, and that secondary metabolites are useful as antibiotics, mycotoxins, insecticides, and herbicides.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the method of library construction of claims 21 and 22 of U.S. Patent No. 5,783,431 by selection for sequences that encode proteins involved in secondary

metabolism because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

11. Claims 27-29, 32-36, and 39-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 8, and 10 of U.S. Patent No. 5,824,485 in view of Vining.

The instant claims are drawn to gene expression libraries comprising constructs comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms. In some embodiments the constructs have been selected for sequences that encode proteins that are involved in secondary metabolism. In some embodiments the donor organism is from an environmental sample, and the library is in a host cell.

Claim 3 of U.S. Patent No. 5,824,485 is drawn to a gene expression library comprising cDNA or genomic DNA fragments isolated from a plurality of species of different organisms, in which the constructs have been selected for a specific property and the constructs are operably linked to elements that allow for expression in a host cell. Claim 8 is drawn to the library of claim 3 in which the species of different organisms are derived from an environmental sample. Claim 10 is drawn to the library of claim 3 in which the constructs comprise metabolic pathway genes. Claims 21 and 22 of U.S. Patent No. 5,783,431 are not drawn to libraries selected for sequences that encode proteins that are involved in secondary metabolism.

Vining shows in the abstract that secondary metabolism genes are preferably isolated from genomes of different organisms because they are of ancient origin and are better conserved between species of organisms than within related genes of the same organism. Vining shows throughout many examples of secondary metabolism genes involved in the synthesis of polyketides, beta-lactams, and erythromycin, and that secondary metabolites are useful as antibiotics, mycotoxins, insecticides, and herbicides.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the library of claims 3, 8, and 10 of U.S. Patent No. 5,824,485 by selection for sequences that encode proteins involved in secondary metabolism because Vining shows that secondary metabolism genes are best obtained from different species of organisms and are useful to make antibiotics, mycotoxins, insecticides, and herbicides.

Conclusion

12. Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. For routine submissions the FAX number is (703) 308-4242. For FAX transmissions in cases in which the Examiner has been notified by phone to expect the transmission, the FAX number is (703) 305-7939. In such cases please call the Examiner at (703) 308-4231 at the time of transmission to expedite delivery of the fax. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6 (d)). NOTE: If

applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, Ph.D., can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

John S. Brusca, Ph.D.

Patent Examiner